

# Tumor model generation and treatment

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Dynamic changes in glioma macrophage populations after radiotherapy reveal CSF-1R inhibition as a strategy to overcome resistance

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## Detailed protocol

### Tumor model generation and treatment

CrI:NU(NCr)-*Foxn1*<sup>nu</sup> immunodeficient mice were purchased from Charles River Laboratories for orthotopic implantation of human cells (U251 and TS573). Nestin-Tv-a;*Ink4a/Arf*<sup>-/-</sup> mice (BL/6 background) and Nestin-Tv-a mice (BL/6 background) have been previously described (12, 14, 16, 17) and were bred within the University of Lausanne (UNIL), Memorial Sloan Kettering Cancer Center (MSKCC), or Netherlands Cancer Institute (NKI) animal facilities. Flk2-switch (*Flt3:Cre*, Rosa26:mTmG) mice were kindly provided by Dr. Camilla Forsberg (University of California-Santa Cruz). Gliomas were initiated by injection of either DF-1 cells expressing an RCAS vector encoding PDGF-B HA in Nestin-Tv-a;*Ink4a/Arf*<sup>-/-</sup> mice (PDG-Ink4a/Arf KO model), or DF-1 cells expressing PDGF-E HA and a short hairpin RNA targeting *TP53* in Nestin-Tv-a mice (PDG-p53 KD and *Flt3:Cre*, Rosa26:mTmG models). All animal studies were approved by the Institutional Animal Care and Use Committees of the UNIL, Canton Vaud, MSKCC, and NKI.

BLZ945 and vehicle (20% Captiso®) formulation and dosing regimen are described in (14, 16). For all combination trials, BLZ945 was administered 30 mins prior to radiotherapy. The Cd49d neutralizing antibody (α-Cd49d) and rat-IgG control antibody were obtained from BioXCell and 200ug was administered every 3 days i.p., starting 3 days prior to fractionated radiation treatment. Temozolomide was administered for 5 days at 50 mg/kg (daily i.p. injections) concurrently with fractionated radiation.

For all fixed time-point studies, mice underwent MRI scans which were measured as previously described (14, 16). Following development of brain tumor symptoms, mice were sedated with isoflurane and irradiation of the head was performed using a X-RAD 320 from Precision X-Ray at 115 cGy/min. Radiation was dosed at 2 Gy/day for five days unless indicated otherwise (e.g. Fig. 1D). Animals were euthanized upon recurrence of the tumor as monitored by regular MRI imaging, or by neurological symptoms, as approved by the Institutional Animal Care and Use Committee of each institute.

**How to cite:** (Readers should cite both the Bio-protocol preprint and the original research article where this protocol was used)

1. Akkari, L. and Joyce, J. (2022). Tumor model generation and treatment. Bio-protocol Preprint. [bio-protocol.org/prep1521](https://bio-protocol.org/prep1521).
2. Akkari, L., Bowman, R. L., Tessier, J., Klemm, F., Handgraaf, S. M., Groot, M. D., Quail, D. F., Tillard, L., Gadiot, J., Huse, J. T., Brandsma, D., Westerga, J., Watts, C. and Joyce, J. A. (2020). Dynamic changes in glioma macrophage populations after radiotherapy reveal CSF-1R inhibition as a strategy to overcome resistance. Science Translational Medicine 12(552). DOI: [10.1126/scitranslmed.aaw7843](https://doi.org/10.1126/scitranslmed.aaw7843)

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